



INTRODUCTION

- Smoking is the primary risk factor for extensive-stage small cell lung cancer (ES-SCLC), yet the impact of cumulative smoking exposure on bispecific T-cell engager (BiTE) outcomes remains unclear.
- We evaluated the association between smoking burden and survival outcomes in patients with ES-SCLC treated with the BiTE tarlatamab.

METHODS

- We conducted a retrospective cohort study of patients with relapsed/refractory ES-SCLC treated with tarlatamab at three academic institutions from June 2024 to January 2026.
- Pack-years at diagnosis were divided into three groups (0-24, 25-49, and ≥50), representative of tobacco use tertiles.
- Primary endpoints were progression-free survival (PFS) and overall survival (OS). PFS and OS were estimated using the Kaplan-Meier method. Univariable Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs).

RETROSPECTIVE MULTI-INSTITUTIONAL COHORT

3 ACADEMIC CENTERS

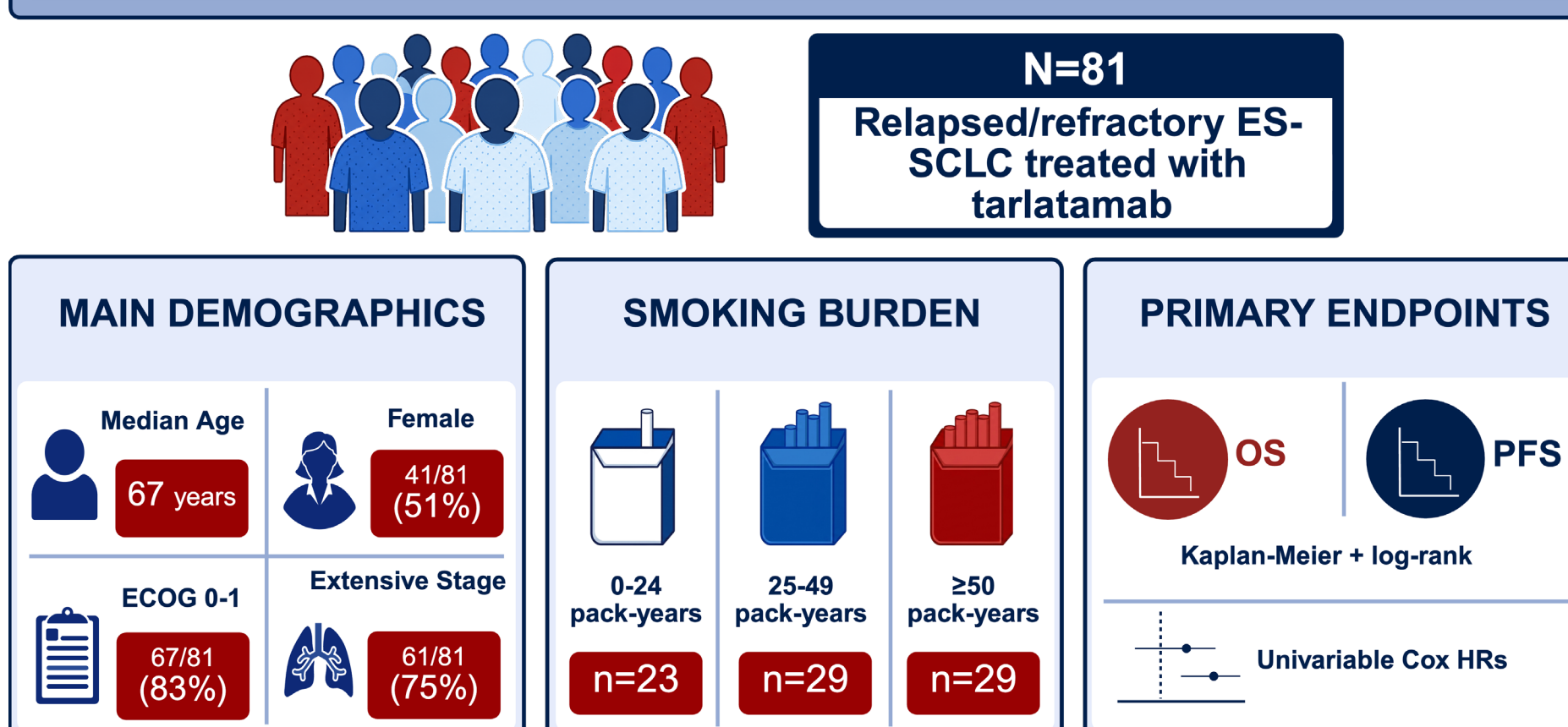


Figure 1. Study cohort and analysis overview.

Table 1. Baseline characteristics by smoking history (pack-years at diagnosis)

Characteristic	0–24 (N=23)	25–49 (N=29)	50+ (N=29)	p-value*
Site				0.30
CU	3 (13%)	2 (7%)	5 (17%)	
Duke	17 (74%)	20 (69%)	14 (48%)	
HFH	3 (13%)	7 (24%)	10 (34%)	
Age at diagnosis, median (IQR)	67 (62, 71)	67 (60, 71)	69 (64, 75)	0.40
Sex				0.095
Female	13 (57%)	18 (62%)	10 (34%)	
Male	10 (43%)	11 (38%)	19 (66%)	
Race/ethnicity				0.20
White	15 (65%)	21 (72%)	25 (86%)	
Black	8 (35%)	6 (21%)	3 (10%)	
Other	0 (0%)	2 (7%)	1 (3%)	
ECOG				0.40
0	5 (22%)	5 (17%)	2 (7%)	
1	16 (70%)	20 (69%)	19 (66%)	
2	2 (9%)	4 (14%)	6 (21%)	
3	0 (0%)	0 (0%)	2 (7%)	
Tarlatamab line of therapy				0.70
2nd line	14 (61%)	15 (52%)	12 (41%)	
3rd line	7 (30%)	9 (31%)	12 (41%)	
≥4th line	2 (9%)	5 (17%)	5 (17%)	
Stage at diagnosis				>0.90
Limited	5 (22%)	8 (28%)	7 (24%)	
Extensive	18 (78%)	21 (72%)	22 (76%)	
Brain metastases at diagnosis				0.60
Yes	5 (22%)	4 (14%)	7 (24%)	
No	18 (78%)	25 (86%)	22 (76%)	

*P-values were calculated using Kruskal–Wallis, chi-square, or Fisher's exact tests as appropriate.

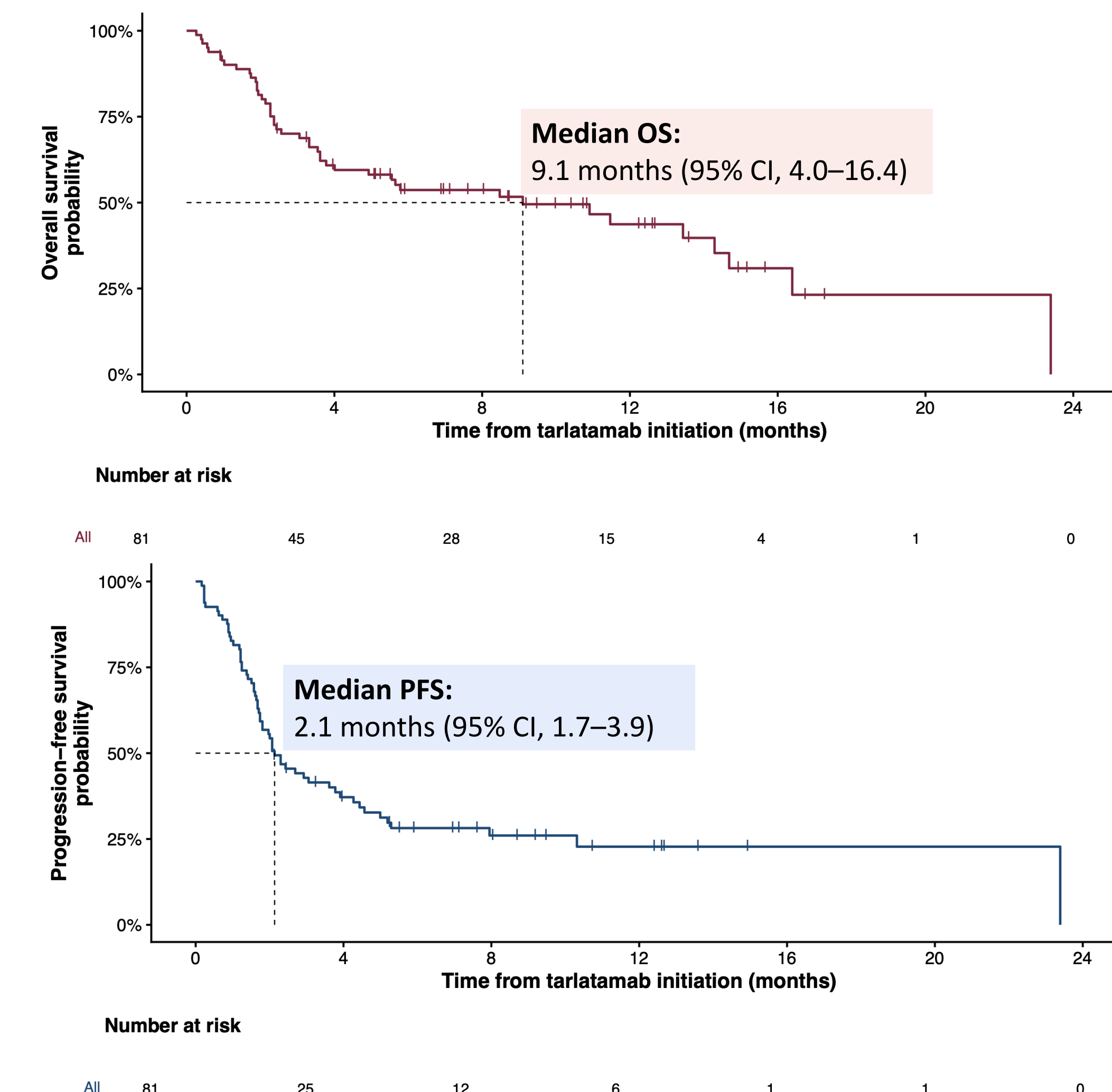


Figure 2. Global cohort OS and PFS.

RESULTS

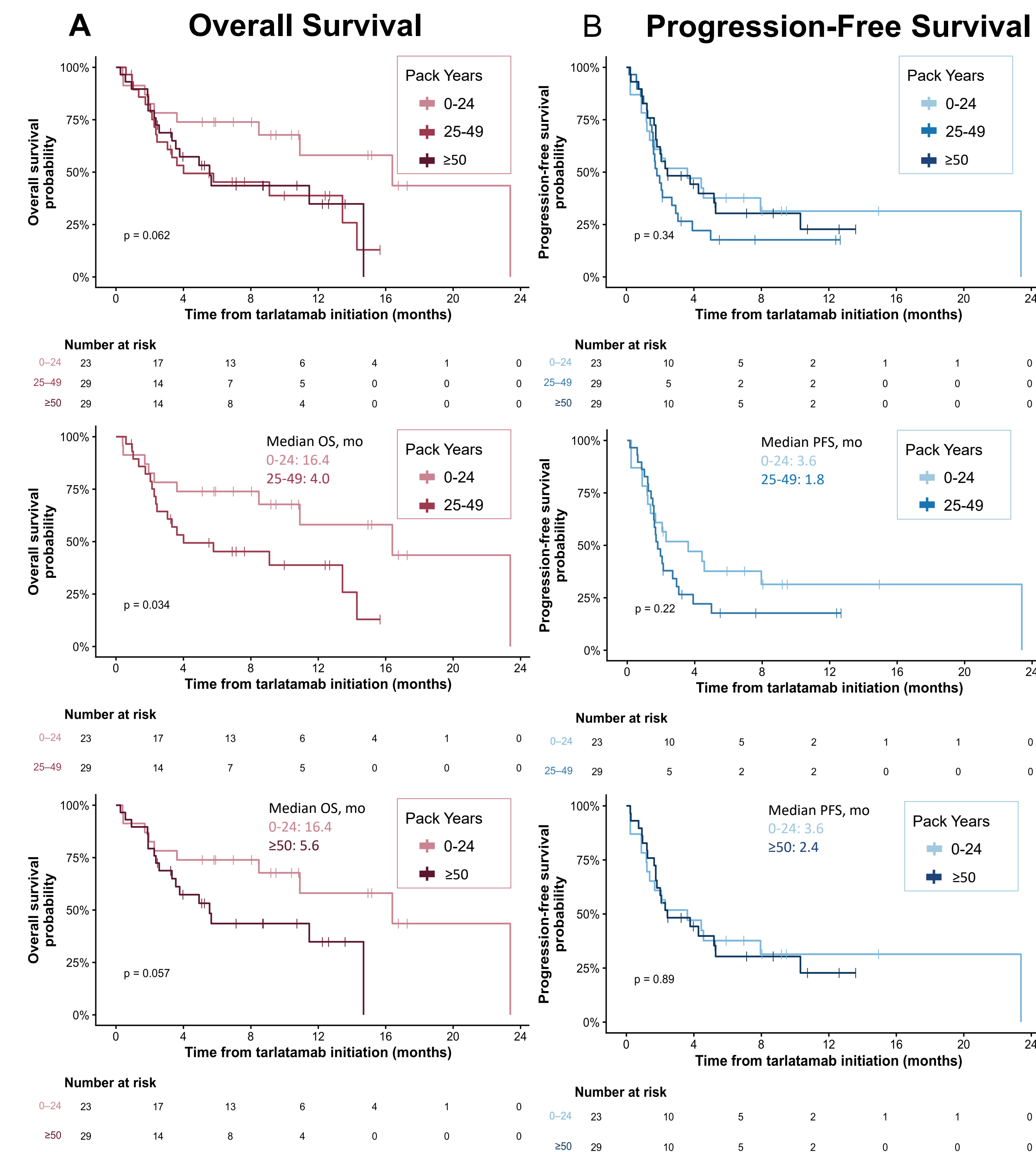


Figure 3. Kaplan–Meier curves of OS (A) and PFS (B) stratified by smoking burden at diagnosis.

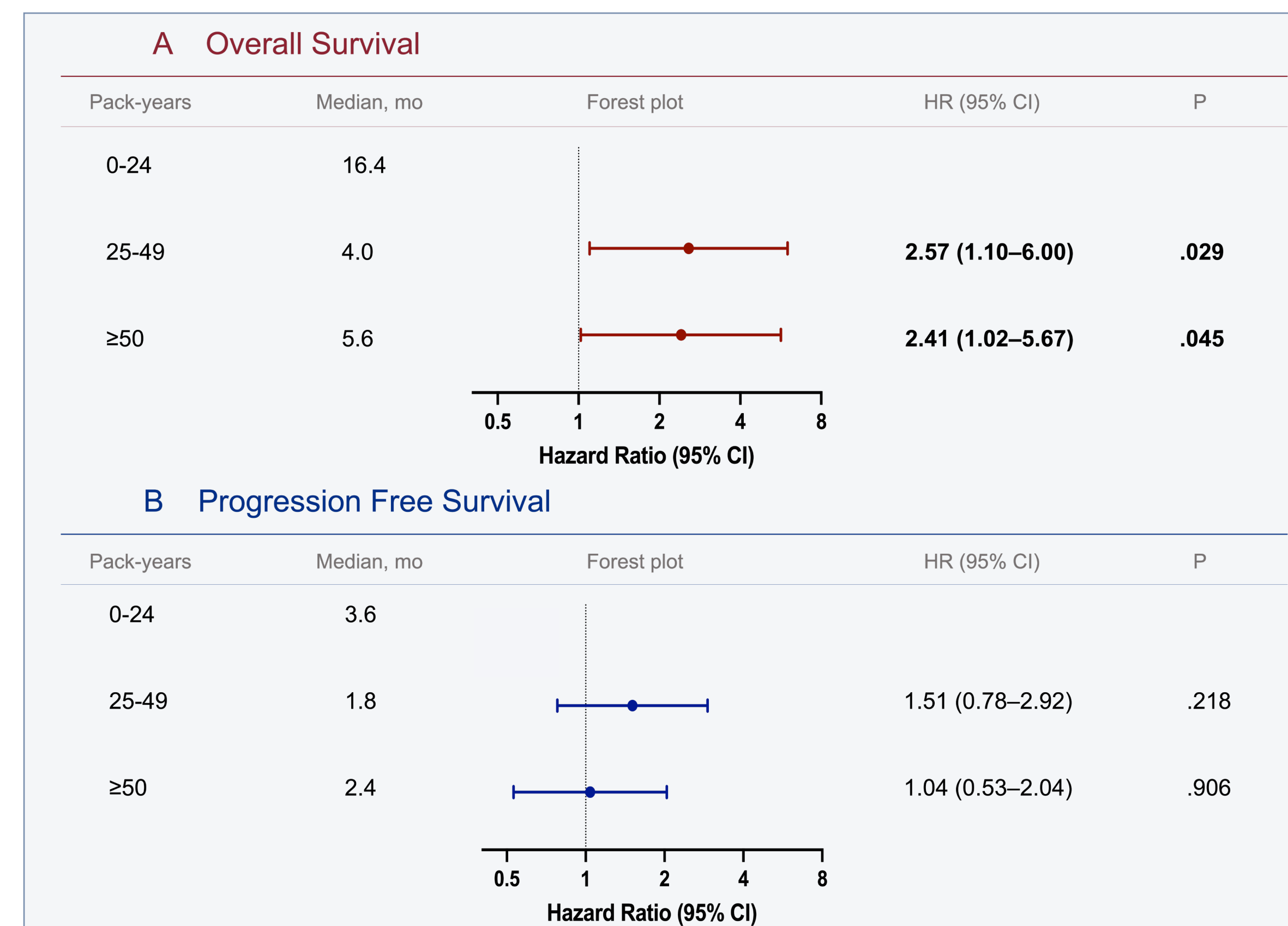


Figure 4. Univariable Cox hazard ratios for OS (a) and PFS (b) by smoking burden. 0-24 pack-years is reference group.

DISCUSSION

- Both higher pack-year groups had significantly higher hazards of death than the 0–24 pack-year group in univariable Cox models. The lowest pack-year group had the longest PFS, but this was not statistically significant.
- Exploratory pairwise Kaplan–Meier analysis demonstrated statistically significant OS separation between the 0–24 and 25–49 pack-year groups, while the comparison between the 0–24 and ≥50 groups was clinically significant but did not reach statistical significance, possibly due to low sample size.
- Prior studies in SCLC have not consistently identified cumulative smoking exposure as an independent adverse prognostic factor outside the immunotherapy setting.
- Our findings raise the possibility that smoking burden may be particularly relevant in the context of BiTE therapy. Whether this reflects differential immune-mediated mechanisms, adverse clinical or biologic features associated with heavier smoking, or other factors warrants further investigation.

REFERENCES & ACKNOWLEDGEMENTS



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